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(71) Applicant (for all designated States except US): **BASF AKTIENGESELLSCHAFT** [DE/DE]; 67056 Ludwigshafen (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **FREUND, Annette** [DE/DE]; Römerweg 17c, 67117 Limburgerhof (DE).
RÖHL, Franz [DE/DE]; Sebastian-Kneipp-Str. 17, 67105

Schifferstadt (DE). **ALTHÖFER, Henning** [DE/DE]; Im Höhnhausen 26, 67157 Wachenheim (DE). **KAROS, Marvin** [DE/DE]; Fröbelstrasse 2, 67433 Neustadt (DE). **KAESLER, Bruno** [DE/DE]; Magdeburger Str. 72, 67071 Ludwigshafen (DE). **LACOUR, Thierry** [FR/DE]; Lutherstr. 4, 76297 Stutensee (DE).

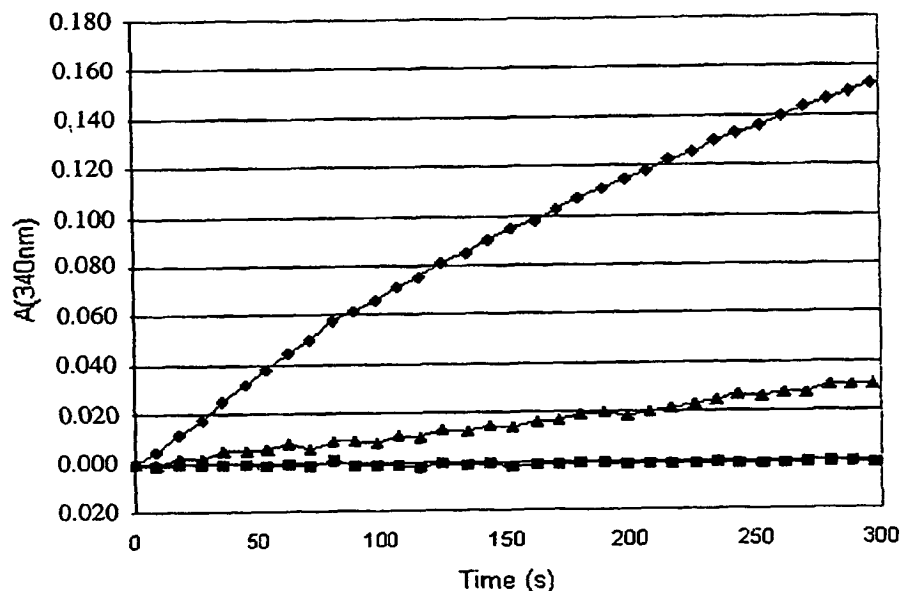
(74) Common Representative: **BASF AKTIENGESELLSCHAFT**; 67056 Ludwigshafen (DE).

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[Continued on next page]

(54) Title: GTP CYCLOHYDROLASE II AS A TARGET FOR FUNGICIDES



(57) Abstract: The present invention relates to inhibition of GTP cyclohydrolase II as target for the identification of fungicides. Binding assays are claimed and coupled enzymatic assays are disclosed involving the conversion of formate (product of the reaction catalyzed by GTP-cyclohydrolases) by formate dehydrogenase and spectroscopically measuring the NADH formed. Furthermore in vivo assays with organisms containing a GTP-cyclohydrolase II are claimed as well as a DNA sequence for a fungal GTP-cyclohydrolase II. 3-Butyl-10-(3-chlorophenyl)-10H-pyrimido[4,5-b]quinoline-2,4-dione is identified by the enzymatic method as a fungicide. Finally, methods of controlling fungi (e.g. on plants, in soil) by applying this agent are claimed.



SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/09369

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12Q1/34 C12Q1/32 C12N15/52 C12N15/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBL, CHEM ABS Data, PAJ, WPI Data, MEDLINE, BIOSIS, FSTA, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 00/40744 A (HERZ STEFAN ;BACHER ADELBERT (DE)) 13 July 2000 (2000-07-13) cited in the application the whole document page 1, line 1 - line 7 page 2, line 21 - line 28 page 4, line 13 -page 5, line 8 page 7, line 19 - line 21 page 14, line 11 - line 27 claims 1,12	1,2, 4-15,17, 19,21
Y	US 5 821 090 A (BUITRAGO SERNA MARIA JOSE ET AL) 13 October 1998 (1998-10-13) abstract column 9, line 1 -column 14, line 37 --- -/-	1,2, 4-11,14, 15,17, 19,21

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

3 May 2004

Date of mailing of the international search report

- 7. 05. 2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Tuynman, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/09369

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BLAU N ET AL: "THE APPLICATION OF 8 AMINO-GTP A NEW INHIBITOR OF GTP CYCLOHYDROLASE I TO THE PURIFICATION OF THE ENZYME FROM HUMAN LIVER" BIOCHIMICA ET BIOPHYSICA ACTA, vol. 880, no. 1, 1986, pages 26-31, XP008014569 ISSN: 0006-3002 abstract ---	1,2,17, 19,21
Y	DATABASE WPI Section Ch, Week 198513 Derwent Publications Ltd., London, GB; Class B04, AN 1985-078062 XP002233356 & JP 60 030696 A (WAKO PURE CHEM IND LTD), 16 February 1985 (1985-02-16) abstract ---	1,2, 4-11,14, 15,17, 19,21
A	RITZ HARALD ET AL: "Biosynthesis of riboflavin: Studies on the mechanism of GTP cyclohydrolase II." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 276, no. 25, 22 June 2001 (2001-06-22), pages 22273-22277, XP002233121 ISSN: 0021-9258 cited in the application the whole document ---	7-11,14
Y	US 6 171 598 B1 (WARD JUDITH M ET AL) 9 January 2001 (2001-01-09) column 1, line 53 - line 65 ---	1,2, 4-11,14, 15,17, 19,21
Y	WO 00/22133 A (NOVARTIS ERFIND VERWALT GMBH ;DIETRICH FRED (CH); NOVARTIS AG (CH)) 20 April 2000 (2000-04-20) the whole document ---	12,13
A	MAIER J ET AL: "Homology cloning of GTP-cyclohydrolase I from fungi and plants by reverse-transcription PCR using a general set of degenerate primers" PTERIDINES 1995 GERMANY, vol. 6, no. 3, 1995, pages 112-115, XP008029120 ISSN: 0933-4807 the whole document -----	3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/09369

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,
all additional fees are to be refunded.

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1-15,17,19,21
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1,2,4-11,14,17,19,21

Methods for identifying antifungal agents involving GTP hydrolase as a target.

1.1. Claims: 1,2,14,17-19,21 (partially)

Binding assay methods for identifying antifungal agents involving GTP cyclohydrolases as a target.

1.2. Claims: 1,2,4,14,17-19,21 (partially); 5-11 (fully)

Enzymatic (cell-free) assay methods for identifying antifungal agents involving GTP cyclohydrolases as a target.

2. Claims: 12,13 (fully) 1,4,14,15,17,19,21 (partially)

In vivo methods for identifying antifungal agents involving GTP hydrolases as a target.

Invention 3: 3 (fully)

Nucleic acid sequences encoding a fungal GTP hydrolase II.

4. Claims: 16,18 (fully)

The antifungal agent
3-butyl-10-(3-chlorophenyl)-10H-pyrimido[4,5-b]quinoline-2,4-dione and the use thereof for producing drugs.

5. Claim : 20 (fully)

Method for controlling harmful fungi.

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/09369

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